Original Article

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Beneficial Role of Vitamin D Supplementation and Clinical Outcomes in Patients with Dengue Fever: A Randomised Controlled Trial

Internal Medicine Section

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ABSTRACT

Introduction: Dengue Fever (DF) continues to be a major public health burden in tropical and subtropical countries. Severe forms such as Dengue Haemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS) are characterised by vascular leak, bleeding, and increased mortality. Vitamin D, with its immunomodulatory and endothelial protective properties, has been proposed as a potential adjunct therapy.

Aim: To evaluate the effect of vitamin D supplementation on clinical outcomes, platelet recovery, and disease severity in hospitalised dengue patients.

Materials and Methods: The present study employed a double-blinded randomised controlled trial over a period of 12 months (from July 2023 to July 2024), included 144 serologically confirmed dengue patients admitted to a tertiary care hospital at Mahatma Gandhi Medical College and Research Institute (MGMCRI), Pondicherry, India. Participants were allocated into two groups: Group A received vitamin D supplementation (2000 IU/day) along with standard care, and Group B received standard care alone. Clinical parameters (bleeding, transfusion requirements, warning signs, ascites, pleural effusion, and shock) and laboratory indices {Platelet Count (PC), Total Count (TC) and Packed Cell Volume (PCV)} were serially monitored. Data were analysed using Statistical Package for the Social Sciences (SPSS) version 25; Mann-Whitney U-test, Wilcoxon signed-rank test, and chi-square test were applied as appropriate ($p<0.05$).

Results: The overall mean age of the study participants was 37.15±12.14 years and majority were male patients (Group A: 49/72; Group B: 42/72). PC increased significantly within both groups from day 0 to day 5 (baseline change +20,811±15,240 (Group A) and +21,234±14,890 (Group B); $p<0.001$) and day 10 (baseline change +77,295±21,445 (Group A) and +75,884±22,156 (Group B); $p<0.001$). However, Group A demonstrated significantly fewer bleeding manifestations (9 vs 36; $p<0.001$), reduced platelet transfusion requirement (7 vs 30; $p<0.001$), and lower incidence of DHF across age and gender subgroup ($p<0.05$). No significant differences were observed in hospital or ICU stay.

Conclusion: Vitamin D supplementation in dengue patients significantly reduced bleeding complications, transfusion needs, and progression to severe dengue, though platelet recovery and hospitalisation outcomes remained unaffected. These findings highlight the potential role of vitamin D as a safe, low-cost adjunct in dengue management, warranting validation through larger multicentric trials.

Keywords: Bleeding manifestation, Cholecalciferol, Dengue shock syndrome, Platelet

INTRODUCTION

Dengue is a rapidly expanding arboviral disease with sustained transmission across the globe. The World Health Organisation (WHO) reports a historic high of >14.6 million cases and >12,000 death in 2024 and continued widespread activity into 2025, with 1.3 billion people living in dengue endemic area in Southeast Asia [1,2]. National surveillance in India also documents substantial year-on-year burden across States/Union Territories (UTs) [3]. These data underscore a persistent global expansion driven by urbanisation, climate variability and vector adaptation, with marked risk of severe disease and health-system strain [2,4]. In dengue, the conventional management primarily focuses on supportive care, particularly judicious fluid resuscitation during the critical phase [4,5], a notable absence remains in specific therapeutic interventions to prevent disease progression. The existence of this treatment gap underscores the necessity for developing innovative strategies to reduce dengue severity and improve clinical outcomes.

Vitamin D acts as a pleiotropic immunomodulator, where the contemporary reviews detail suppression of NF-κB-driven cytokines, promotion of regulatory T-cells, and down-regulation of T helper 1 (Th1)/T helper 17 (Th17) responses, alongside enhancement of innate antimicrobial functions [6-8]. Collectively, these mechanisms support a biologically plausible role of vitamin D in infections characterised by dysregulated inflammation.

Recent evidence suggests that host nutritional status, particularly vitamin D levels, may significantly influence dengue pathogenesis and severity [9,10]. Vitamin D Deficiency (VDD), defined as serum 25(OH)D levels below 20 ng/mL, has been implicated as a potential risk factor for developing severe dengue [11]. Additionally, observational studies have documented inverse relationships between serum 25(OH)D levels and the risk of infection particularly severe bleeding and progression to DHF or DSS [12,13]. Moreover, paediatric data from India similarly suggest protective effects of sufficiency [13].

Given the convergence of high dengue burden and prevalent hypovitaminosis D in tropical populations, coupled with mechanistic plausibility and early clinical signals, rigorous interventional evidence is needed. Prior studies are limited by observational design, small samples, or heterogeneity of dosing and timing [12-16]. The dosage for the present study was selected based on evidence that it can rapidly achieve and sustain therapeutic 25(OH)D levels above 30ng/mL [16] while remaining well below the established safety threshold of 4000 IU daily [11,17-19].

The present randomised, controlled study aimed to evaluate whether daily 2,000 IU cholecalciferol as an adjunct to standard care improved clinical outcomes in confirmed dengue, specifically in platelet recovery, vascular-leak manifestations and progression to severe disease, thereby addressing a clinically relevant and scalable strategy for resource-limited settings.

The primary objectives of the study were to supplement hospitalised dengue patients with oral vitamin D (2000 IU/day) for 10 days or for the duration of their hospital stay, and to assess its effect on clinical outcomes. Following the secondary objectives include to classify patients according to clinical severity as DF without Warning Signs (DF), Dengue Fever with Warning Signs (DFWS) and DHF and to evaluate the clinical profile during hospitalisation.

MATERIALS AND METHODS

The current study was a double-blinded randomised controlled trial conducted at the Department of General Medicine, Mahatma Gandhi Medical College and Research Institute (MGMCRI), Pondicherry, India, for a period of 12-months (from July 2023 to July 2024). The study was approved by the Institutional Human Ethics Committee (IHEC) of MGMCRI (MGMCRI/Res/01/2022/93/IHEC/29). All participants provided written informed consent after receiving an explanation of the study procedures, potential risks, and expected benefits. The trial adhered to the ethical standards of 1964 Helsinki Declaration and its subsequent amendments. Ethical clearance and patient autonomy were prioritised to ensure the integrity of research and compliance with international clinical trial regulations (CTRI/2023/10/059167).

Sample size calculation: The sample size was calculated based on the findings from the study by Iqtadar S et al., (2023), which reported an estimated prevalence of epistaxis one of the bleeding manifestations among vitamin D-deficient dengue patients was 15.5% [16].

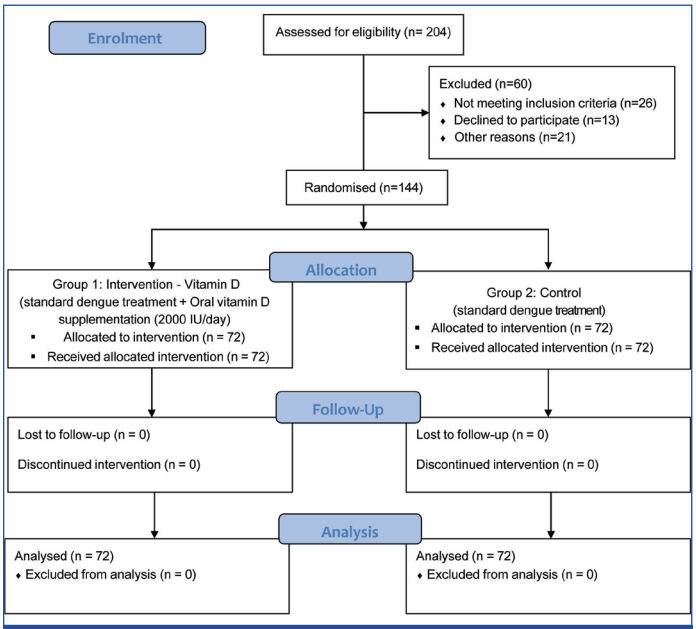
Using the formula {n = $(Z^2_1$-a/2×p×(1-p)/$d^2)$ = $(1.96)^2$*0.155*(1-0.155) /$(0.12)^2$=35.94~36, where Z_1-a/2=1.96 (at 95% Confidence Level (CI)), p (prevalence)=0.155, and d (precision at 12%) = 0.12}, the minimum sample size calculated was 36 cases per group. To account for loss to follow-up, protocol deviation, and non-evaluable cases in an acute infectious disease setting, we anticipated up to 50% drop-out and calculated using $n_{adjusted}$ =n/(1-r)=36/(1-0.50)=72 participants per group. Thus, the final sample size was set at 144 participants.

Inclusion criteria: Adults aged 18-60 years of either sex with laboratory-confirmed dengue infection (positive NS1 antigen by rapid card test) and patients with or without warning signs, bleeding manifestations, or vascular leak.

Exclusion criteria: Participants were excluded from the study if they presented with any comorbidities other than Diabetes Mellitus (DM) and systemic hypertension, co-infections (e.g., scrub typhus, malaria), haematological disorders {Thrombotic Thrombocytopenic Purpura (TTP), haemolytic uremic syndrome, Disseminated Intravascular Coagulation (DIC), Idiopathic Thrombocytopenic Purpura (ITP)}, any current use of antiplatelet drugs or anticoagulants and required for platelet transfusion, any chronic kidney or liver disease and pregnant or lactating mothers.

Study Procedure

Randomisation and blinding: Block randomisation was employed to allocate participants into two equal groups. The random allocation sequence was generated by an independent statistician from Department of Community Medicine who was not involved in participant recruitment or clinical care, using a computer-based random number generator. The sequence was concealed in sequentially numbered, opaque, sealed envelopes prepared by a study coordinator not involved in enrolment. Eligible participants were screened and enrolled into the study by the investigators from the Department of General Medicine after confirming eligibility and obtaining written informed consent. Following enrolment and completion of baseline assessment, the attending physician opened the next envelope in sequence and assigned the participant to the allocated groups as Group A (Intervention): Standard dengue treatment plus oral vitamin D supplementation (cholecalciferol 2000 IU/day) [20] for 10 days or until hospital discharge and Group B (Control): Standard dengue treatment alone. Laboratory personnel processing the blood samples and the statistician performing the data analysis were blinded to group allocation [Table/Fig-1].



[Table/Fig-1]: CONSORT flow diagram.

Vitamin D supplementation: The intervention group received commercially available vitamin D tablets (cholecalciferol 2000 IU IP) once daily for 10 consecutive days or until discharge if earlier. This dosage was selected based on Central European Guidelines 2013, as it provides sufficient supplementation to achieve 25(OH) D levels of at least 75nmol/L (30ng/mL) without risk of toxicity [20]. Administration was directly observed by nursing staff during hospitalisation.

Standard dengue treatment: All participants in both groups received standard dengue treatment according to WHO guidelines [21], which included judicious fluid resuscitation with crystalloids, antipyretics (paracetamol) for fever management, regular monitoring of vital signs and warning signs, serial haematological investigations and supportive care as required. All clinical and laboratory data were recorded using a pre-structured proforma. Baseline evaluation done on admission (day 0), with a detailed clinical history and physical examination performed. Demographic characteristics, clinical manifestations and outcome of the treatment were recorded. Laboratory investigations included TC, PC, and PDW. Patients were categorised as DF, DFWS, or DHF according to WHO criteria (2009) [21]. During hospitalisation, serial haemograms were obtained on day 0, day 5, and day 10 or at discharge. PC were monitored on those days and TC and PDW were also assessed.

In addition, the following were assessed daily including clinical status (dehydration, abdominal pain, persistent vomiting, mucosal bleeding, hepatomegaly), evidence of vascular leak such as pleural effusion and ascites (detected clinically and confirmed by chest X-ray or ultrasonography), warning signs or progression to severe dengue, need for platelet transfusion, Intensive Care Unit (ICU) admission, or ventilatory support. Also, comprehensive safety assessment and tolerability profile were done. All these ensured real-time monitoring of disease progression and timely interventions as per standard protocols.

Study Outcomes: Primary outcome was the clinical improvement and progression to severe dengue with platelet recovery pattern, while the secondary outcomes as changes in clinical profile, duration of hospital stay, occurrence of bleeding manifestations, development of vascular leak, requirement for platelet transfusion, and need for ICU admission or ventilator support.

STATISTICAL ANALYSIS

Statistical analysis was performed using IBM SPSS Statistics software (version 25.0). Normality of the data was assessed using Shapiro-Wilk test. Continuous variables were expressed as mean±Standard Deviation (SD) or median {Interquartile Range (IQR)} depends on the distribution of the variable and compared using Mann-Whitney U-test or Wilcoxon signed rank test; while the categorical variables were expressed as frequencies and percentages, compared using Chi-square test or Fisher's exact test. Subgroup analyses were performed to assess the differential effects of vitamin D supplementation. A p-value of <0.05 was considered statistically significant.

RESULTS

The demographic characteristics of the study participants were presented in [Table/Fig-2], with the mean age 37.15±12.14 years overall, and were statistically non-significant. Both groups were comparable, confirming effective randomisation. Both groups demonstrated significant platelet recovery during hospitalisation. Patients were classified based on the severity of the disease as DF, DFWS, and DHF in both groups and found to be statistically significant [Table/Fig-3]. Also, there was a substantial reduction in DHF incidence showing a remarkable 76.7% Relative Risk (RR) reduction in DHF development (9.7% vs 41.7%, p<0.001) in Group A.

Variables		Group A n=72 n (%)	Group B n=72 n (%)	p-value*
Age (in years)	45-60	22 (30.6)	23 (31.9)	0.971
	25-45	36 (50.0)	36 (50.0)	
	18-25	14 (19.4)	13 (18.1)	
Gender	Male	49 (68.1)	42 (58.3)	0.233
	Female	23 (31.9)	30 (41.7)	

[Table/Fig-2]: Demographic characteristics of the study participants.
*Pearson's Chi-square test. p-value <0.05 were statistically significant and indicated in boldface.

Variables	Group A (n=72)	Group B (n=72)	p-value
DF	32 (44.4)	16 (22.2)	<0.001*
DFWS	33 (45.8)	26 (36.1)	
DHF	7 (9.7)	30 (41.7)	

[Table/Fig-3]: Disease severity of dengue among the study participants.
*Pearson's Chi-square test. p-value <0.05 - statistically significant and indicated in boldface. DF: Dengue fever without warning signs; DFWS: Dengue fever with warning signs; DHF: Dengue haemorrhagic fever.

[Table/Fig-4] shows the platelet recovery trajectory where at baseline (day 0), the mean PC were comparable between the two groups and were statistically non-significant. By day 5, both groups demonstrated significant increase in PC compared with day 0 (p<0.001). A further significant rise was observed by day 10/discharge (p<0.001). The percentage of improvement from baseline to day 5 and day 10/discharge were clinically improved yet, statistically non-significant. However, between-group comparison at day 5 and day 10 did not reveal statistically significant differences. Also, with no between-group difference in absolute counts or percentage of recovery (p>0.4).

Clinical manifestation and outcome of the treatment were presented in [Table/Fig-5], showed that bleeding manifestation and requirement of platelet transfusion were significantly reduced in Group A when compared to Group B and statistically significant (p<0.001 for both). While the rest of the clinical outcomes were reduced yet statistically non-significant.

Subgroup analysis of demographic with dengue severity were done and found to be statistically significant [Table/Fig-6]. Comparison of major clinical outcomes between both groups are presented in [Table/Fig-7].

Variables	Group A (n=72)	Group B (n=72)	p-value*	
			Within-group	Between-group
PC (cells/mm³)				
Day 0 (baseline)	29,447±16,616	28,335±14,986		0.715[a]
Day 5	50,258±18,226	49,569±17,318		0.792[a]
Change from baseline	+20,811±15,240	+21,234±14,890	<0.001[b]	
% Improvement	+70.7	+74.9		0.848[a]
Day 10/ discharge	106,742±17,988	104,219±19,148		0.429[a]
Change from baseline	+77,295±21,445	+75,884±22,156	<0.001[b]	
% Improvement	+262.4	+267.8		0.990[a]
TC (cells/mm³)	5,700 (4,000-6,800)	5,700 (4,000-6,800)		0.893[a]
PCV (%)	43 (42-45)	45 (43-47)		0.063[a]

[Table/Fig-4]: Platelet Count (PC) recovery trajectory and haematological parameters among the study participants.
[a]Mann-Whitney U-test; [b]Wilcoxon Signed rank test. p-value <0.05 were statistically significant and indicated in boldface. PCV: Packed cell volume; TC: Total count; PC: Platelet count. Data were presented as mean±Standard Deviation (SD) or median (IQR) based on the distribution and normality of the data. Improvement provided as percentage

Variables	Group A (n=72)	Group B (n=72)	p-value
Evidence of warning signs	36 (50.0)	42 (58.3)	0.403[a]
Bleeding manifestations	9 (12.5)	36 (50.0)	<0.001[a]
Requirement of platelet transfusion	7 (9.7)	30 (41.7)	<0.001[a]
Plasma leakage syndrome			
Evidence of ascites	24 (33.3)	26 (36.1)	0.861[a]
Evidence of pleural effusion	28 (38.9)	28 (38.9)	1.000[a]
Evidence of shock	14 (19.4)	18 (25.0)	0.548[a]
Ventilator requirement	0 (0.0)	1 (1.4)	1.000[a]
Duration of hospital stay (in days)	5.0 (4.0-7.0)	5.0 (4.0-9.2)	0.937[b]
Duration of ICU stay (in days)	2.0 (1.0-3.0)	1.5 (0.8-3.0)	0.101[b]
Recovered	72 (100.0)	72 (100.0)	1.000[a]

[Table/Fig-5]: Clinical manifestations and outcome of the treatment for the dengue among the study participants.
[a]Pearson's Chi-square test or Fisher's-Exact test (based on the cell values); [b]Mann-Whitney U-test. p-value <0.05 were statistically significant and indicated in boldface. Data were presented as frequency (percentage) or median (interquartile range) depends on the type of variables and distribution

Comprehensive safety assessment and tolerability profile provided in [Table/Fig-8].

DISCUSSION

In the present double-blinded RCT, adjunct vitamin D (2000 IU/day) significantly reduced progression to DHF, bleeding manifestations, and platelet transfusion requirements compared with standard care alone, while overall recovery was 100% with no mortality. However, the platelet recovery trajectory and hospital/Intensive Care Unit (ICU) stay were comparable between groups, suggesting benefit primarily on clinical severity and haemostatic or endothelial stability rather than platelet kinetics alone. The mechanism was the vitamin D and its effect on the DENV replication, and the haemostatic and vascular protective effects were presented in the [Table/Fig-9].

A key finding was the marked reduction in DHF in the vitamin D arm amounting to a 76.7% RR reduction, indicating that vitamin D may help prevent escalation to severe disease, while DF/DF with warning signs constituted the remainder, supporting its potential role in vitamin D in limiting progression to severe phenotypes [21]. This direction is consistent with clinical literature linking lower 25(OH)D levels with greater dengue severity and haemorrhagic risk, where deficiency has been associated with more severe clinical

Variables		Group A n=72			Group B n=72			p-value*
		DF (n=32)	DFWS (n=33)	DHF (n=7)	DF (n=16)	DFWS (n=26)	DHF (n=30)	
Age (in years)	45-60	10 (31.3)	8 (24.2)	4 (57.1)	3 (18.8)	8 (30.8)	12 (40.0)	<0.001
	25-45	17 (53.1)	17 (51.5)	2 (28.6)	10 (62.5)	13 (50.0)	13 (43.3)	<0.001
	18-25	5 (15.6)	8 (24.3)	1 (14.3)	3 (18.7)	5 (19.2)	5 (16.7)	<0.001
Gender	Male	23 (71.9)	21 (63.6)	5 (71.4)	9 (56.3)	18 (69.2)	15 (50.0)	<0.001
	Female	9 (28.1)	12 (36.4)	2 (28.6)	7 (43.7)	8 (30.8)	15 (50.0)	<0.001

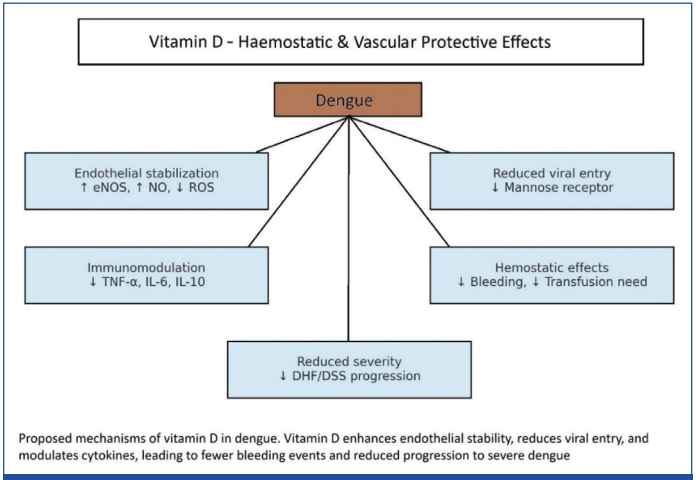
[Table/Fig-6]: Subgroup analysis of demographic with the dengue classification for both groups of patients.
*Pearson's Chi-square test. p-value <0.05 were statistically significant and indicated in boldface. DF: Dengue fever without warning signs; DFWS: Dengue fever with warning signs; DHF: Dengue haemorrhagic fever

Outcome	Group A (n=72) n (%)	Group B (n=72) n (%)	Relative Risk (RR) reduction with vitamin D vs control (%)	p-value*
Dengue Haemorrhagic Fever (DHF)	7 (9.7)	30 (41.7)	76.7%	<0.001
Any bleeding manifestation	9 (12.5)	36 (50.0)	75.0%	<0.001
Platelet transfusion required	7 (9.7)	30 (41.7)	76.7%	<0.001
Recovery (discharged alive)	72 (100)	72 (100)	-	-
Mortality	0 (0)	0 (0)	–	–

[Table/Fig-7]: Comparison of major clinical outcomes between both groups.
Pearson's Chi-square test or Fisher's Exact test; p-value <0.05 is statistically significant and represented in boldface.

Variables	Group A (n=72) n (%)	Group B (n=72) n (%)
Vitamin D - related adverse event		
Hypervitaminosis symptoms	0 (0)	0 (0)
Gastrointestinal intolerance	0 (0)	0 (0)
Treatment compliance		
Complete supplementation course	72 (100.0)	72 (100.0)
Treatment discontinuation	0 (0)	0 (0)
Serious Adverse Events (SAE)		
Treatment - related SAE	0 (0)	0 (0)
Mortality	0 (0)	0 (0)

[Table/Fig-8]: Comprehensive safety assessment and tolerability profile.



[Table/Fig-9]: Mechanism of the haemostatic and vascular protective effects of vitamin D in dengue.

presentations [14]. A nested case-control study in Colombia found that low serum 25(OH)D levels were associated with increased Odds Ratio (OR) of progression from DF to DHF or DSS with adjusted OR were 0.44 and 0.13 for insufficiency and deficiency (p=0.003) [22]. Regional evidence also reports a high burden of VDD among dengue patients and a tendency towards worse severity among those with lower levels, supporting biological plausibility for supplementation benefits [16]. Mechanistic studies describe vitamin D-mediated immunomodulation that may reduce the exaggerated inflammation implicated in vascular permeability and severe dengue manifestations [11,12]. Randomised trial by Zaman S et al., demonstrated that vitamin D significantly lowered progression to DHF and DSS, highlighting its role as a vascular protective adjunct in dengue management [23].

In the present trial, PC improved significantly over time in both groups from Day 0 to day 5 and further to day10/discharge, reflecting the expected convalescent rise seen with supportive dengue care [18,21]. Despite this improvement, between-group differences in PC and overall recovery slope were not significant, indicating that vitamin D did not measurably accelerate platelet regeneration [18,21]. This trajectory is consistent with guideline description that thrombocytopenia typically worsens around the critical phase or defervescence and then recovers during the recovery phase, often paralleling clinical stabilisation [18,24,25]. Pathogenesis reviews explain dengue thrombocytopenia as multifactorial bone marrow suppression, immune mediated platelet destruction, and increased peripheral consumption/separation with recovery occurring as viral or immune injury resolves and haematopoiesis rebounds [6,8].

Importantly, our finding of similar platelet recovery but reduced bleeding or transfusion need in the vitamin D arm supports the concept that bleeding risk is not determined by PC alone [14,21,26]. This aligns closely with cohort evidence showing that low vitamin D status is associated with severe bleeding not fully explained by thrombocytopenia, suggesting potential effects on endothelial or haemostatic pathways rather than PC [10,14].

In the present study, TC was identical between groups, indicating no measurable effect of vitamin D on leukocyte counts during hospitalisation. This is compatible with dengue's typical haematologic course normalise with clinical recovery under supportive care, so Group level differences may be hard to detect [6,18]. This closely matches with the hospitalised adult dengue cohort from Lahore reported by Iqtadar S et al., where the TC on admission was $4.7*10^9$/L, with similarly overlapping values in vitamin D-deficient vs sufficient groups [16].

Similarly, PCV was slightly lower in the vitamin D arm but not statistically significant, suggesting no clear between-group difference in haemoconcentration. WHO dengue guidance emphasises rising haematocrit or PCV as a marker of plasma leakage, and the lack of the significant PCV separation in our trial aligns with the generally comparable leakage-related outcomes between groups [21]. Iqtadar S et al., reported a median haematocrit 43%. Overall, again, it is very similar to the present study PCV range, without meaningful differences by vitamin D status (43.6% vs 43%) [16]. From a clinical standpoint, WHO-based frameworks emphasise haemoconcentration (~>20% rise in haematocrit) as a marker of significant plasma leakage rather

than small absolute PCV difference, which supports why the present study modest PCV separation did not translate into major leakage-related outcome differences [21,27].

Clinically, vitamin D supplementation was associated with fewer bleeding manifestation and markedly lower platelet transfusion requirements indicating a clinically important reduction in haemorrhagic complications [21]. Other manifestations related to plasma leakage and shock/ventilator requirement were not significantly different, and hospital/ICU stay was similar, reinforcing that the primary treatment signal was on bleeding or DHF prevention [18]. Safety outcomes were reassuring with no vitamin-D related events, full compliance, and zero treatment-related serious adverse events, consistent with established vitamin D safety standards or guidance at commonly used doses [20]. Compared to published cohorts, the control-group bleeding rate (50%) in the present study is higher than the overall haemorrhagic manifestation rate reported in Singapore by Sadarangani SP et al., (28.8%). Another cohort reported an inverse trend between systemic 25(OH)D levels and dengue severity, particularly for bleeding manifestations not explained by thrombocytopenia [14]. In a multicentre randomised trial, Lye DC et al., found clinical bleeding in 21% of transfusion vs 26% of control patients (no significant difference), but adverse events were higher with transfusion (13 vs two events), and there were no deaths, supporting strategies that reduce unnecessary transfusion exposure [28].

According to the study by Rusińska A et al., comparing between the 1000IU and 2000IU vitamin D supplementation, results showed a sharp rise in vitamin D levels with 2000 IU/day and sustained over a longer period of time, relatively [29]. Since the study had to be done within a short course of patient stay in the hospital, 2000 IU/day dose of vitamin D was chosen as a prophylactic dose as per Central Europe Guidelines 2013 [20], which helps in rapid rise in vitamin D compared to 1000 IU/day after analysing the safety profile. Vitamin D supplementation at 2000 IU/day demonstrated an exemplary safety profile with zero adverse events, complete patient tolerance, and no laboratory abnormalities. This safety profile supports clinical implementation after a large-scale multicentric trial, given the observed substantial therapeutic benefits. While our results are encouraging, larger multicentric trials are warranted to confirm these benefits, define optimal dosing strategies, and explore their applicability across different dengue serotypes and severity spectra.

Limitation(s)

First, the single-centre design and the specific demographic profile of the enrolled patients may limit the external validity, particularly in regions with different dengue serotype prevalence or population characteristics. Second, baseline vitamin D levels were not measured, limiting mechanistic interpretation and preventing determination of whether observed benefits reflected correction of deficiency versus effects independent of baseline status; future studies should incorporate baseline vitamin D assessment and dose-response evaluation. Finally, the cohort was predominantly adult population, the findings may not be directly generalisable to paediatric or elder patients who may have different clinical trajectories and risk profiles.

CONCLUSION(S)

Adjunctive vitamin D supplementation in hospitalised adults with dengue infection substantially reduced progression to DHF and haemorrhagic complications compared with standard care alone. The need for platelet transfusion was also markedly lower in the vitamin D group, suggesting better preservation of haemostatic function and less demand on blood bank resources. Despite the higher-risk profile of patients with dengue, overall recovery was 100% with no mortality in either arm, reflecting both effective supportive care and a potential additional benefit of vitamin D. These findings support a plausible immunomodulatory and endothelial-stabilising role of vitamin D in modifying the clinical course of dengue.

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